

10/821,657 filed 04/08/2004

Wada et al.

Reply to Office Action of 07/24/2006

**REMARKS/ARGUMENTS**

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Claims 1–93 are pending in the above-captioned application. Claims 1–4, 6, 8–44, 51–79, 81, and 83–93 stand rejected, and claims 5, 7, 45–50, 80, and 82 are withdrawn from consideration. With this paper, claims 1, 31, 32, 36–42, 51, 55, 56, and 93 have been amended, claims 30, 45–50, 52, and 54 have been canceled, and claims 94–100 have been added. No new matter was added with the amendment.

**I. Election/Restrictions**

Applicants elected to prosecute the invention of Group I (claims 1–44 and 51–93), electing the species heparin sulfate from the subgenus polyanionic polymers. Claims 5, 7, 80, and 82 are withdrawn as being drawn to a nonelected subgenus (polycationic polymers). Claims 45–50 are withdrawn as being drawn to a nonelected invention (Group II). To simplify prosecution of this case, Applicants are canceling claims 45–50, while retaining the right to pursue those claims in a divisional application. Cancellation of the non-elected claims does not necessitate an amendment to the inventorship.

**II. Claim rejections under 35 U.S.C. § 112, second paragraph**

Claims 30–32, 39–41, 42, 52, and 54–56 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Each of the Examiner's reasons for rejecting claims 30–32, 39–41, 52, and 54–56 has been addressed in the amendments to the still-pending claims.

Claims 30–32 were rejected because the Examiner objected to the phrase “further comprises” in claim 30. Claim 30 has been canceled. Claims 31 and 32, which originally depended from claim 30, have been amended to depend from claim 1. Neither claim 31 nor claim 32 contains the phrase “further comprises.”

Claims 39–41 were rejected because they were alleged to be “unclear with regard to which analyte is labeled.” Applicants have amended claim 39 to clarify that three materials are contacted: 1) the sample containing the analyte of interest, 2) *either* the analyte of interest labeled by a detectable marker *or* an analogue of the analyte of interest labeled by a detectable

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marker, and 3) an affinity molecule. Applicants respectfully assert that, in the context of the amended claim, the analyte in the sample and the labeled analyte are clearly separate entities (i.e., separate quantities of the same analyte of interest). Only separate entities can be contacted one with another as recited in the claim. Claim 40 has been amended to clarify that three materials are contacted: 1) the sample containing the analyte of interest, 2) *either* the labeled analyte of interest *or* the labeled analogue of the analyte of interest, and 3) a conjugate of the affinity molecule and a charged carrier molecule. Claim 41 has been amended to clarify that four materials are contacted: 1) the sample containing the analyte of interest, 2) *either* the labeled analyte of interest *or* the labeled analogue of the analyte of interest, 3) the affinity molecule, and 4) a conjugate of the affinity molecule and a charged carrier molecule.

Claim 42 was rejected based on the allegation that it "is unclear with regard to what the sample containing the analyte is contacting." Applicants have amended claim 42 to clarify that three materials are contacted: 1) the sample containing the analyte of interest, 2) *either* the analyte bound to a charged carrier molecule *or* an analogue of the analyte bound to a charged carrier molecule, and 3) an affinity molecule labeled by a detectable marker.

Claims 52 and 54 were rejected based on the allegation that the claims are unclear and that the term "slower" in claim 54 is a relative term, rendering the claim indefinite. Both claims have been canceled.

Claims 55 and 56 were rejected as allegedly having insufficient antecedent basis for the term "the noise constituents." In each of these claims, the phrase "the noise constituents" has been replaced with the phrase "noise constituents in the sample."

With the above-described amendments, Applicants respectfully assert that claims 31, 32, 39-41, 42, 55, and 56 should be found to comply with the requirements of 35 U.S.C. § 112, second paragraph.

To simplify and add further clarity to claims 36-42, limitations directed to two or more affinity molecules, or two or more conjugates of an affinity molecule and a charged carrier molecule, have been separated out from the original claims and presented as new dependent claims 94-100. No new matter was added by removing the limitations from the original claims and presenting them in new dependent claims.

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**III. Claim rejections under 35 U.S.C. § 102(b) as being anticipated by Kawabata et al. (EP 1376126A1) as evidenced by Walston et al. (US 2001/0055591)**

Claims 1–3, 6, 9–29, 33, 35–44, 51–55, 59–65, 67–78, 81, 83, 85, 86, 90, 92, and 93 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kawabata et al. (EP 1376126A1) as evidenced by Walston et al. (US 2001/0055591). This rejection is respectfully traversed. “[F]or anticipation under 35 U.S.C. § 102, a single reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present.” MPEP § 706.02. “The identical invention must be shown in as complete detail as is contained in the . . . claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, USPQ2d 1913, 1920 (Fed. Cir. 1989).

With regard to independent claims 1, 39, 42, and 93, at a minimum, Kawabata et al. do not teach a separation channel in a microfluidic device “filled with a separation media and a charged polymer.” The limitation in quotation marks has been added to claims 1, 39, and 42 to more particularly point out and distinctly claim Applicants’ invention. Support for the limitation can be found throughout the specification, for example on page 16, lines 32 and 33; on page 17, line 34, through page 18, line 1; and on page 40, line 21; as well as in original claim 30. Thus, no new matter has been added by the amendment.

At most, Kawabata et al. teach adding a charged polymer to a liquid containing nucleic acid chain-binding affinity substances. The charged polymer acts as a nuclease inhibitor. Kawabata et al. teach on page 12, paragraphs 0057–0061, regarding a molecular sieving material packed inside a capillary. However, the reference is silent with regard to adding the charged polymer to the sieving material in a separation channel in a microfluidic device to produce a separation channel that is filled with both a separation medium and a charged polymer.

With regard to claim 51, at a minimum, Kawabata et al. do not teach a concentration channel in a microfluidic device “filled with a concentration media and a charged polymer.” The limitation in quotation marks has been added to claim 51 to more particularly point out and distinctly claim Applicants’ invention. Support for the limitation can be found, for example, on page 65, lines 29–34, and on page 73, line 33. Thus, no new matter has been added by the amendment.

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As described by the Examiner on page 10 of the Office action, Kawabata et al. teach using capillary electrophoresis to migrate a sample through a first capillary for introduction into a second capillary for separation. The Examiner has identified this first capillary as a concentration channel. In paragraph 0056 on page 12, Kawabata et al. state that a "buffer for migration (electrophoresis) is packed in" the first capillary. Kawabata et al. are silent with regard to a capillary filled with both a concentration medium and a charged polymer.

Thus, Kawabata et al. do not teach every aspect of the claimed invention either explicitly or impliedly, nor do they show the identical invention claimed by Applicants in as complete detail as is contained in independent claims 1, 39, 42, 51, and 93. Withdrawal of the rejection of claims 1, 39, 42, 51, and 93 under § 102(b) as being anticipated by Kawabata et al. is, therefore, respectfully requested.

Claims 2, 3, 6, 9-29, 33, 35-38, 43, and 44 depend directly or indirectly from amended independent claim 1; claims 40 and 41 depend directly from amended independent claim 39; and claims 53-55, 59-65, 67-78, 81, 83, 85, 86, 90, and 92 depend directly or indirectly from amended independent claim 51. Please note that claims 22, 37, and 38 have been amended to maintain consistency with amended claims 1 and 39, from which they depend. Applicants respectfully submit that claims 2, 3, 6, 9-29, 33, 35-38, 40-44, 53-55, 59-65, 67-78, 81, 83, 85, 86, 90, and 92 are allowable for at least the same reasons as set forth herein with respect to amended independent claims 1, 39, and 51. Withdrawal of the rejection of these dependent claims § 102(b) as being anticipated by Kawabata et al. is also respectfully requested. As noted previously, claim 52 has been canceled.

Applicants wish to point out that the Walston et al. reference was cited on page 6 of the present Office action for the sole purpose of providing evidence that "heparin is a polysaccharide with a strong negative charge." The Examiner has not alleged that Walston et al. teach regarding a separation channel in a microfluidic device that is filled with a separation media and a charged polymer, nor does the reference provide this teaching.

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IV. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1) in view of Bickel et al. (Proc. Natl. Acad. Sci.)

Claims 4, 8, 79, and 84 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kawabata et al. (EP 1376126A1) in view of Bickel et al. (Proc. Natl. Acad. Sci., Vol. 89, pp. 10001–10005, November 1992). The rejection of these claims is respectfully traversed.

To warrant rejection under 35 U.S.C. § 103(a), all the claim limitations must be taught or suggested by the prior art. *See* MPEP § 2142. As demonstrated above, Kawabata et al. neither teach nor suggest all of the limitations of Applicants' amended independent claims 1 and 51, from which claims 4, 8, 79, and 84 depend. Thus, claims 1 and 51 are nonobvious over the Kawabata et al. reference.

Bickel et al. do not teach a separation channel in a microfluidic device filled with a separation media and a charged polymer, the feature demonstrated above to be absent from the teachings of Kawabata et al. At most, Bickel et al. teach adding heparin sulfate (a charged polymer) to protein extracts in a binding buffer, this buffer mixture then being loaded onto a standard polyacrylamide gel for electrophoretic separation. *See* the first column of page 10002. Therefore, Applicants' amended independent claims 1 and 51 are nonobvious over the combination of Kawabata et al. and Bickel et al.

Claims 4 and 8 depend directly and indirectly, respectively, from amended independent claim 1, while claims 79 and 84 depend indirectly from amended independent claim 51. Any claim depending from a nonobvious claim is also nonobvious. *See* MPEP § 2143.03 and *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, dependent claims 4, 8, 79, and 84 are nonobvious. Withdrawal of the rejection of these claims over Kawabata et al. in view of Bickel et al. is, therefore, respectfully requested.

V. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1) in view of Stathakis et al. (Journal of Chromatography)

Claims 30–32 and 87–89 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kawabata et al. (EP 1376126A1) in view of Stathakis et al. (Journal of

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Chromatography A, Vol. 817, pp. 227–232, 1998). The rejection of these claims is respectfully traversed.

As demonstrated above, claims 1 and 51, from which claims 30–32 and 87–89 depend, are nonobvious over Kawabata et al. Stathakis et al. do not teach a separation channel in a microfluidic device filled with a separation media and a charged polymer, the feature demonstrated above to be absent from the teachings of Kawabata et al. At most, Bickel et al. teach adsorbing a charged polymer, i.e., dextran sulfate or poly(vinyl sulphonic acid), to a capillary wall, thereby minimizing protein-wall interactions during electrophoretic separation of proteins in food samples. As is made clear in section 2.2, in the second column of page 228, the capillary contains no separation medium and is not “filled” with a charged polymer, the polymer being adsorbed to the inner wall of the capillary. Thus, Applicants’ amended independent claims 1 and 51 are nonobvious over the combination of Kawabata et al. and Stathakis et al.

Claims 31 and 32 depend directly from amended independent claim 1, while claims 87–89 depend indirectly from amended independent claim 51. As any claim depending from a nonobvious claim is also nonobvious, dependent claims 31, 32, and 87–89 are nonobvious. Withdrawal of the rejection of these claims over Kawabata et al. in view of Stathakis et al. is, therefore, respectfully requested. As noted previously, claim 30 has been canceled.

**VI. Claim rejections under 35 U.S.C. § 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1) in view of Stalcup et al. (Analytic Chemistry)**

Claims 34 and 91 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kawabata et al. (EP 1376126A1) in view of Stalcup et al. (Analytic Chemistry, Vol. 66, pp. 3054–3059, 1994). The rejection of these claims is respectfully traversed.

As demonstrated above, claims 1 and 51, from which claims 34 and 91 depend, are nonobvious over Kawabata et al. Stalcup et al. do not teach a separation channel in a microfluidic device filled with a separation media and a charged polymer, the feature demonstrated above to be absent from the teachings of Kawabata et al. At most, Stalcup et al. teach 2% heparin in a phosphate run buffer used for capillary zone electrophoresis. The capillary contains no separation medium, per the “Apparatus” section in column 2 of page 3054. Thus,

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Applicants' amended independent claims 1 and 51 are nonobvious over the combination of Kawabata et al. and Stalcup et al.

Claim 34 depends indirectly from amended independent claim 1, while claim 91 depends indirectly from amended independent claim 51. As any claim depending from a nonobvious claim is also nonobvious, dependent claims 34 and 91 are nonobvious. Withdrawal of the rejection of these claims as unpatentable over Kawabata et al. in view of Stalcup et al. is, therefore, respectfully requested.

**VII. Claim rejection under 35 U.S.C. § 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1) in view of Fukui et al. (Nucleic Acids Research)**

Claim 66 was rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kawabata et al. (EP 1376126A1) in view of Fukui et al. (Nucleic Acids Research, Vol. 24, No. 20, pp. 3962-3967, 1996). The rejection of these claims is respectfully traversed.

As demonstrated above, claim 51, from which claim 66 depends, is nonobvious over Kawabata et al. Fukui et al. do not teach a separation channel in a microfluidic device filled with a separation media and a charged polymer, the feature shown above to be missing from the teachings of Kawabata et al. At the bottom of page 3962, continuing on to the top of page 3963, Fukui et al. teach a high performance liquid chromatography (HPLC) method carried out using a COSMOSIL AR-300 column (4.6 x 150 mm). Thus, Fukui et al. do not teach a separation channel in a microfluidic device or a charged polymer that, along with a separation medium, fills such a separation channel. Therefore, Applicants' amended independent claim 51 is nonobvious over the combination of Kawabata et al. and Fukui et al.

Claim 66 depends indirectly from amended independent claim 51. As any claim depending from a nonobvious claim is also nonobvious, dependent claim 66 is nonobvious. Withdrawal of the rejection of claim 66 as unpatentable over Kawabata et al. in view of Fukui et al. is, therefore, respectfully requested.

Applicants respectfully note that the Fukui et al. reference was not listed on the Examiner's "Notice of References Cited" nor was a copy of the reference posted on the USPTO's Patent Application Information Retrieval (PAIR) Web site.

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**BEST AVAILABLE COPY**Conclusion

For the foregoing reasons, Applicants believe all the pending claims are in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned attorney.

Respectfully submitted,



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